

## AMENDMENTS TO THE CLAIMS

Claims 1 – 44 (cancelled)

45. (Currently Amended) A low-volume hybridization device, comprising:  
a base,

a pressure chamber,

a reaction chamber disposed in said base, said reaction chamber being bound by  
a flexible diaphragm separating said pressure chamber from said reaction chamber, and

a probe array disposed in said reaction chamber for hybridization, said pressure  
chamber and said flexible diaphragm being constructed to change a volume of said  
reaction chamber by application of pressure or vacuum and thereby facilitate said  
hybridization.

46. (Previously presented) The low-volume hybridization device of claim 45,  
wherein said reaction chamber has a volume in the range of 0.1 to 100  $\mu\text{l}$ .

47. (Previously presented) The low-volume hybridization device of claim 45,  
wherein said reaction chamber has a volume in the range of 1 to 20  $\mu\text{l}$ .

48. (Currently Amended) The low-volume hybridization device of claim 45,  
further comprising:

a pneumatic system for providing said pressure or vacuum to said pressure  
chamber and thereby moving said flexible diaphragm.

49. (Original) A hybridization device, comprising:

a base,

a fluidic chamber disposed in said base, said fluidic chamber having a  
hybridization array disposed therein,

a porous membrane disposed in said fluidic chamber opposite said array,

a pneumatic port disposed in said base, said pneumatic port addressing said porous membrane, and  
a thermal control device for controlling the temperature in the array.

Claims 50 – 65 (Cancelled)

66. (Previously Presented) The low-volume hybridization device of claim 45 including an addressable heater thermally coupled to said reaction chamber.

67. (Previously Presented) The low-volume hybridization device of claim 66 including a thermal insulation in contact with said heater.

68. (Previously Presented) The low-volume hybridization device of claim 66 including a temperature sensor positioned adjacent said heater.

69. (Previously Presented) The low-volume hybridization device of claim 45, including a cooler thermally coupled to said reaction chamber.

70. (Previously Presented) The low-volume hybridization device of claim 69, wherein said cooler is a thermoelectric cooler.

71. (Previously Presented) The low-volume hybridization device of claim 45 further including an extraction chamber constructed and arranged to exchange fluids with said reaction chamber.

72. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a porous flow-through plug having nucleic acid binding properties.

73. (Previously Presented) The low-volume hybridization device of claim 72, wherein said plug is a deformable plug.

74. (Currently Amended) The low-volume hybridization device of claim 73, further including a second wherein said flexible diaphragm associated with said deformable plug and [[is]] constructed and arranged to compress said deformable plug for removing trapped liquids.

75. (Previously Presented) The low-volume hybridization device of claim 72, wherein said plug comprises glass wool.

76. (Previously Presented) The low-volume hybridization device of claim 72, wherein said plug is pretreated with an agent for enhancing the nucleic acid binding properties.

77. (Previously Presented) The low-volume hybridization device of claim 76, wherein said agent is selected from the group consisting of acids, bases, silanes, polysine, tethered antibodies, synthesized nucleic acids, and Poly-T DNA.

78. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a textured surface having nucleic acid binding properties.

79. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a structure comprising an open cell foam.

80. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes an affinity surface having particles attached thereto, the particles having nucleic acid binding properties.

81. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface includes controlled-pore glass structures.

82. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface has glass spheres attached thereto.

83. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface has cellulose particles attached thereto.

84. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface is microfabricated.

85. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface is machined.

86. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface is injection molded.

87. (Previously Presented) The low-volume hybridization device of claim 45 further including a base-unit including a manifold constructed and arranged to control said flexible diaphragm.

88. (Previously Presented) The low-volume hybridization device of claim 87 wherein said manifold is a vacuum manifold.

89. (Previously Presented) The low-volume hybridization device of claim 87 wherein said base-unit further includes flow connectors for delivering fluid to said reaction chamber.

90. (Previously Presented) The low-volume hybridization device of claim 87 wherein said base-unit further includes electrical connectors for controlling operation within said device.

91. (Currently Amended) A low-volume hybridization device, comprising:

a base,

a pressure chamber,

a reaction chamber disposed in said base, said reaction chamber being bound by a flexible diaphragm separating said pressure chamber from said reaction chamber,,

a probe array disposed in said reaction chamber for hybridization, said pressure chamber being constructed for application of pressure or vacuum to said flexible diaphragm to enable fluid displacement in said reaction chamber for achieving hybridization, and

a processing chamber connectable to said reaction chamber and constructed for exchanging fluids with said reaction chamber.

92. (Currently Amended) The low-volume hybridization device of claim 91 including a pneumatic manifold constructed and arranged to provide pressure or vacuum to said pressure chamber to displace ~~deflect~~ said flexible diaphragm. ~~for exchange fluids between said reaction chamber and said processing chamber.~~

93. (Previously Presented) The low-volume hybridization device of claim 92 wherein said processing chamber includes an amplification chamber.

94. (Previously Presented) The low-volume hybridization device of claim 93 wherein said amplification chamber is constructed for PCR amplification.

95. (Previously Presented) The low-volume hybridization device of claim 92 wherein said processing chamber includes a sample acquisition chamber.

96. (Previously Presented) The low-volume hybridization device of claim 92 wherein said processing chamber includes an extraction chamber.

97. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a porous flow-through plug having nucleic acid binding properties.

98. (Previously Presented) The low-volume hybridization device of claim 97, wherein said plug is a deformable plug.

99. (Currently Amended) The low-volume hybridization device of claim 98, further including a second wherein said flexible diaphragm associated with said deformable plug and [[is]] constructed and arranged to compress said deformable plug for removing trapped liquids.

100. (Previously Presented) The low-volume hybridization device of claim 97, wherein said plug comprises glass wool.

101. (Previously Presented) The low-volume hybridization device of claim 97, wherein said plug is pretreated with an agent for enhancing the nucleic acid binding properties.

102. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a textured surface having nucleic acid binding properties.

103. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a structure comprising an open cell foam.

104. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes an affinity surface having particles attached thereto, the particles having nucleic acid binding properties.

105. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface includes controlled-pore glass structures.

106. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface has glass spheres attached thereto.

107. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface has cellulose particles attached thereto.

108. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface is microfabricated.

109. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface is machined.

110. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface is injection molded.